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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/580,748	08/11/2006	Patrick Gerard Johnston	36290-0415-00-US	1280

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EXAMINER	
SCHNIZER, RICHARD A	
ART UNIT	PAPER NUMBER
1635	

MAIL DATE	DELIVERY MODE
06/23/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/580,748	JOHNSTON ET AL.	
	Examiner	Art Unit	
	Richard Schnizer	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 March 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15 and 29-52* is/are pending in the application.

4a) Of the above claim(s) *1-15,29,40,41,45 and 46* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *30-39,42-44 and 47-52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 May 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Sequence Listing Validation Report*.

DETAILED ACTION

An amendment was received and entered on 3/26/09.

Election/Restrictions

Applicant has pointed out an error in the previous Action regarding the restriction requirement and claim rejoinder. To clarify, the previous indication that the species requirement for "chemotherapeutic agent" was withdrawn was correct. Both claims 34 and 35 should have been examined, and in fact, were examined, however the Examiner inadvertently omitted claim 35 from the rejection under 35 USC 103 over Hyer, Uslu, Ni, and Tuschl. The indication that claims 34 and 35 were withdrawn was in error.

Claims 1-15, 29, 40, 41, 45 and 46 stand withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 06/10/2008.

Claims 30-39, 42-44 and 47-52 are under consideration.

This action is NON-FINAL due to new grounds of rejection not necessitated by amendment.

Priority

The instant application is the national phase of PCT/GB2004/005006, filed 11/26/04, and claims priority to GB 0327499.0 and GB 0327493.3, each filed 11/26/03. Neither of the foreign priority documents supports instant SEQ ID NO: 2, which is

embraced by all the claims under consideration. Therefore the effective filing date of the instant claims is 11/26/04.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. See page 51, line 12. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Specification/Compliance with Sequence Rules

A substitute sequence listing was received and entered on 4/20/09. The sequence listing was found to be defective for the reasons listed in the attached Validation Report.

Applicant must provide:

An substitute computer readable form (CRF) copy of the "Sequence Listing".

An substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

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For questions regarding compliance to these requirements, please contact:

• For Rules Interpretation, call (571) 272-0951

• For Patentin Software Program Help, call Patent EBC at 1-866-217-9197 or directly at 703-305-3028 / 703-308-6845 between the hours of 6 a.m. and 12 midnight, Monday through Friday, EST.

• Send e-mail correspondence for Patentin Software Program Help @ ebc@uspto.gov.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 30, 34-39, 49 and 50 are rejected under 35 U.S.C. 102(a) as being anticipated by Iwase et al (Int. J. Cancer 106: 619-625, 2003, of record).

Iwase taught that the chemotherapeutic agents cisplatin (CDDP) and 5-FU inhibited expression of c-FLIP (see abstract and Fig. 4). Thus each of these drugs is both a c-FLIP inhibitor and a chemotherapeutic agent. The culture medium comprising the drugs is considered to be a pharmaceutical composition. Thus Iwase anticipates the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 30, 31, 34, 36-39, 42, and 47, and 49-52 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Siegmund et al (Molecular Medicine 8(11): 725–732, 2002, of record), Wajant et al (US 20040126791), and Xiang et al (Oncogene 21: 3611-3619, 2002).

Siegmund taught that tumor cell sensitivity to TRAIL-induced apoptosis could be enhanced by treatment with siRNA directed to c-FLIP.

Wajant taught compositions and methods for treating TRAIL-resistant cancer cells including treatment with c-FLIP siRNAs, apoptosis inducing drugs, and chemotherapeutics. See abstract, paragraphs 12, 17, 18, 55-58, 64-66, and 72.

Xiang taught that tumor cell sensitivity to TRAIL-induced apoptosis could be enhanced by treatment with CPT-11.

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the siRNA of Siegmund with the CPT-11 of Xiang in order to form a composition for the treatment of tumors. One would have been motivated to do so in order to obtain the art-recognized benefit of each component in enhancing TRAIL-induced apoptosis of tumor cells. It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to

form a third composition to be used for the very same purpose. The idea of combining them flows logically from their having been individually taught in the prior art. See MPEP 2144.06(I).

Regarding claims 36 and 37, the ratio of c-FLIP siRNA and chemotherapeutic agent is considered to be a result effective variable that is routinely optimized by those of ordinary skill.

Regarding claims 38 and 39, absent evidence to the contrary, the extent to which p53 is inactivated and the precise identity of the p53 mutation have no effect on the nature of the claimed composition, and receive no patentable weight.

Regarding claims 42, 51, and 52, it would have been obvious to one of ordinary skill in the art at the time of the invention to organize the siRNA of Siegmund and the CPT-11 of Xiang into a kit because one of skill in the art appreciates that organizing experimental reagents prior to use is standard laboratory practice which reduces the frequency of errors.

Regarding claims 49-52 and the limitation requiring the absence of a death receptor binding member, it would have been obvious to formulate the composition or kit either with or without a death domain binding member (such as TRAIL). This is simply a matter of design choice. On the one hand, it would be simple and efficient to administer all three molecules (siRNA, CPT-11, and TRAIL) in one composition, thereby limiting the number of invasive administrations. On the other hand, one it would also be obvious to administer the siRNA and CPT-11 first in order to place the target tumor cells

in a state in which they are maximally responsive to TRAIL when it is administered separately later.

Thus the invention as a whole was prima facie obvious.

Ni et al (US 7,452,538)

Claims 30-39, 42, 47, and 49-52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hyer et al. (Cancer Biology and Therapy, Vol. 1 (4), pp.401-406, 2001), Uslu et al. (Clin. Cancer Res., Vol. 3(6), pp.963-972, 1997), Ni et al. (US 20050244857) and Tuschl et al (US 7,056,704).

The claims are drawn to a composition comprising a c-FLIP inhibitor, a chemotherapeutic agent, the CH11 antibody, wherein the c-FLIP inhibitor is RNAi comprising either SEQ ID NO:1 or 2.

Hyer taught a method of killing DU145 prostate cancer cells comprising administration of a c-FLIP antisense oligonucleotide and CH11 antibody (see Fig. 5).

Uslu taught the treatment of DU145 prostate cancer cells with chemotherapeutic agents (CDDP, adriamycin and Etoposide) followed by anti-FAS CH-11 treatment resulted in synergistic cytotoxicity and apoptosis.

Ni taught a method for treating cancer comprising administering to an individual an antibody that binds to a TRAIL receptor, and a chemotherapeutic agent. Among the chemotherapeutic agents that could be administered were CDDP, 5-FU, CPT-11, oxaliplatin, and Cisplatin. See paragraphs 283, 333, 338-341, 527, and 547.

Tuschl stated that "siRNAs are extraordinarily powerful reagents for mediating gene silencing" and that "siRNAs are effective at concentrations that are several orders of magnitude below the concentrations applied in conventional antisense or ribozyme gene targeting experiments." See column 23, lines 15-20.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to prepare a composition comprising the c-FLIP antisense and CH11 antibody taught by Hyer, and a chemotherapeutic agent as taught by Uslu or Ni. One would have been motivated to do so in order to obtain the art-recognized benefit of each component in treating tumors. It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose. The idea of combining them flows logically from their having been individually taught in the prior art. See MPEP 2144.06(I). It would have been obvious to use any of the chemotherapeutic agents of Uslu or Hyer because these were disclosed as useful in combination with anti-Fas antibodies. MPEP 2144.07 indicates that the selection of a known material based on its suitability for its intended use supports the determination of prima facie obviousness. MPEP 2144.06 indicates that when it is recognized in the art that elements of an invention can be substituted, one for the other, while retaining essential function, such elements are art-recognized equivalents. An express suggestion to substitute one equivalent component or process for another is not necessary to render such substitution obvious. In re Fout, 675 F.2d 297, 213 USPQ 532

(CCPA 1982). In this case it was clearly recognized that CPT-11, f-FU, and cisplatin were all chemotherapeutic agents.

Further, it would have been obvious to one of ordinary skill in the art at the time of the invention to substitute siRNA for the antisense of Hyer. One would have been motivated to do so in order to take advantage of the increased efficacy noted by Tuschl.

Regarding claims 42, 51, and 52, it would have been obvious to one of ordinary skill in the art at the time of the invention to organize the siRNA of Tuschl/Hyer and the CPT-11 of Ni into a kit because one of skill in the art appreciates that organizing experimental reagents prior to use is standard laboratory practice which reduces the frequency of errors.

Regarding claims 49-52 and the limitation requiring the absence of a death receptor binding member, it would have been obvious to formulate the composition or kit either with or without a death domain binding member (such as CH-11). This is simply a matter of design choice. On the one hand, it would be simple and efficient to administer all three molecules (siRNA, CPT-11, and CH-11) in one composition, thereby limiting the number of invasive administrations. On the other hand, one it would also be obvious to administer the siRNA and CPT-11 first in order to place the target tumor cells in a state in which they are maximally responsive to death receptor stimulation by CH-11 when it is administered separately later.

Thus the invention as a whole was prima facie obvious.

Claims 43, 44, and 48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Siegmund et al (Molecular Medicine 8(11): 725–732, 2002), Wajant et al (US 20040126791), and Xiang et al (Oncogene 21: 3611-3619, 2002) as applied to claims 30, 31, 34, 36-39, 42, 47, and 49-52 above, and further in view of Tuschl et al(1) (US 20040259247) and Tuschl et al(2) (The siRNA User Guide. 4/16/03, 6 pages).

Siegmund, Wajant, and Xiang can be combined to render obvious a composition comprising CPT-11 and an siRNA directed against c-FLIP.

These references do not teach an siRNA comprising either SEQ ID NO: 1 or SEQ ID NO: 2. Siegmund did teach an siRNA that overlapped with instant SEQ ID NO: 2 by nine nucleotides (underlined):

```
Instant SEQ ID NO: 1                5′-AAGCAGTCTGTTCAAGGAGCA-3′
Siegmund dsRNA-F2 (908-928 of GenBank U97074)   5′-CAAGGAGCAGGGACAAGTTAC-3′
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Tuschl (1) provided extensive teaching on siRNAs their design, and their use in inhibiting a selected target gene. Tuschl taught that siRNA provides enhanced efficacy compared to prior art compounds (paragraph 8, for example). The entire document is directed to the design and use of siRNA.

Tuschl (2) taught that there were ample providers of siRNA in the art at the time of invention, and that there was also a publicly available computer program to find siRNAs for a given target. Tuschl (2) also provided ample guidance on the design of siRNA compounds. It is noted that the specification discloses at page 51 that a publicly available, prior art siRNA design tool was used to design SEQ ID NOS: 1 and 2.

Since the prior art taught inhibition of c-FLIP using an siRNA overlapping instant SEQ ID NO: 1, it is clear that the general region targeted by SEQ ID NO: 1 was of interest to those of ordinary skill. It would have been obvious to one of ordinary skill in the art at the time of the invention to synthesize other siRNAs in the immediate vicinity in an attempt to optimize performance, and it would have been obvious to arrive at an siRNA comprising or consisting of instant SEQ ID NO: 1 through such routine optimization. It is noted that the methods taught in the prior art may not predict with 100% accuracy which siRNA compounds will inhibit c-FLIP, however, with the use of the prior art algorithms, basic teachings, and siRNA vendors, it would have been routine to make and test siRNA compounds targeted to c-FLIP in the region corresponding to SEQ ID NO: 1. The instant specification provides no evidence that the claimed siRNAs have unexpected properties. The invention as a whole would therefore have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Claims 30-39, 42, and 49-52 are rejected under 35 U.S.C. 102(a) as being anticipated by Iwase et al (Int. J. Cancer 106: 619-625, 2003, of record).

Iwase taught that the chemotherapeutic agents cisplatin (CDDP) and 5-FU inhibited expression of c-FLIP (see abstract and Fig. 4). Thus each of these drugs is both a c-FLIP inhibitor and a chemotherapeutic agent. The culture medium comprising the drugs is considered to be a pharmaceutical composition. Thus Iwase anticipates the claims. Thus Iwase anticipated and rendered obvious claims 30, 34-39, 49 and 50.

Iwase also disclosed treatment of cells with CH-11 and either or both of cisplatin and 5-FU. See abstract and Fig. 3. Therefore it would have been obvious to one of ordinary skill in the art to make a pharmaceutical composition comprising CH-11 and one or both of cisplatin and 5-FU in order to simplify administration of the drugs to the cells of Iwase.

Regarding claims 42, 51, and 52, it would have been obvious to one of ordinary skill in the art at the time of the invention to organize the 5-FU and/or cisplatin of Iwase into a kit because one of skill in the art appreciates that organizing experimental reagents prior to use is standard laboratory practice which reduces the frequency of errors.

Thus the invention as a whole was prima facie obvious.

Response to Arguments

Applicant's arguments filed 6/15/09 have been fully considered but they are not persuasive.

Applicant addresses the rejections over Siegmund and Xiang (now including Wajant) at pages 10-14 of the response. First, Applicant argues that Siegmund teaches away from the combined use of chemotherapeutic drugs and TRAIL-based therapy because Siegmund teaches that c-FLIP-targeted therapies are more specific for sensitizing tumor cells to TRAIL than chemotherapy. This is unpersuasive because the Wajant reference, wherein three of the five inventors are authors on the Siegmund reference, indicates at paragraphs 72 and 73 that a method for treating cancer

comprises administering a pharmaceutical composition using dsRNAs against c-FLIP and an apoptosis-inducing drug such as TRAIL can be used in combination with chemotherapy. The fact that Siegmund indicated that chemotherapy causes side effects, and that such side-effects might be reduced through the use of siRNA, does not mean that one of ordinary skill would not consider using the two together in one method, as clearly suggested by Wajant. Disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. See MPEP 2123, citing *In re* Susi, 440 F.2d 442, 169 USPQ 423 (CCPA 1971). "A known or obvious composition does not become patentable simply because it has been described as somewhat inferior to some other product for the same use." *In re* Gurley, 27 F.3d 551, 554, 31 USPQ2d 1130, 1132 (Fed. Cir. 1994).

Applicant then argues that the invention is not obvious because it results in synergism, relying for support on the specification at page 62, lines 17-28; page 63, lines 25-32; page 67, lines 5-20; and page 68, line 28 to page 69, line 10; and Figs. 11,B, 10C, 12A-C, and 13C. These passages allegedly provide evidence that the effects of FT (FLIP-targeted) siRNA combined with any of the chemotherapeutic drugs oxaliplatin, CPT-11, or 5-FU, resulted in synergistic effects on the amount of cells undergoing apoptosis. This is unpersuasive for at least two reasons. Evidence of unexpected results must be commensurate in scope with the claims (MPEP716.02(d)). In this case, one of the specification passages relied upon for support indicates that several FLIP- targeted siRNAs were tested, but that one potently down-regulated expression of both c-FLIP splice variants in HCT116p53$^{+/+}$ cells at nanomolar

concentrations. Thus it a appears that a single siRNA was used in the experiments relied on for evidence of unexpected results, but these passages do not disclose the identity of this siRNA. For example, it is unclear if the siRNA comprised either of SEQ ID NOS: 1 or 2. Furthermore, none of the rejected claims limits the identity of the c-FLIP inhibitor to siRNA. Note that claims 43, 44, and 48 embrace any RNAi agent comprising or consisting of SEQ ID NOS: 1 or 2. One of skill in the art could construe this as embracing miRNA, shRNA, and even antisense RNA alone. Claim 47 embraces any RNAi agent, and the rest of the claims under consideration embrace any c-FLIP inhibitor at all. Thus none of the claims under consideration is limited to whatever agent was used in the specification to produce the alleged unexpected results.

Applicant argues at page 13 that claims 49-52 are distinguished over the combination of Siegmund and Xiang art because these claims exclude a death receptor binding member, such as TRAIL. This is unpersuasive. The fact that the cited art renders obvious the combined use of c-FLIP siRNA, a death receptor binding member such as TRAIL, and a chemotherapeutic, does not mean that all compositions rendered obvious by the method must comprise TRAIL. One of ordinary skill in the art, aware of the cited references, could make compositions comprising one or more of these three agents, in any combination, for use in treating cancer. That is, one could combine the siRNA and the chemotherapeutic in one composition for use in the method of Siegmund or Wajant, and administer TRAIL separately. It is simply a matter of design choice. Therefore the cited references do not teach away from the compositions of claims 49-52. Applicant also appears to argues that it is unexpected that a composition

comprising a chemotherapeutic agent will kill tumor cells. This is unpersuasive because it is unsupported by evidence.

At pages 13 and 14, Applicant argues that RNAi agents comprising SEQ ID NOS: 1 or 2 are not obvious because employing algorithms and methods in the prior art does not guarantee that the siRNA sequences designed will have any activity. This is unpersuasive because it was apparent from the prior art that an siRNA targeting the region corresponding to SEQ ID N: 1 was active. This would indicate to one of ordinary skill that that particular region of the mRNA was accessible for inhibition by siRNA. Accordingly, in the process of routine optimization, it would be obvious to focus on this region, because it was a certainty that an siRNA overlapping SEQ ID NO: 1 was active. Applicant appears to argue unexpected results with regard to SEQ ID NOS: 1 and 2, indicating that these were extremely potent compared to other siRNA molecules. This allegation is unsupported. The specification indicates that several "FLIP targeted" (FT) siRNAs were tested and that one was superior. See page 62. It does not identify this superior siRNA as either SEQ ID NO: 1 or SEQ ID NO: 2. There is also no evidence that any difference was of statistical significance, which is required to support an argument of unexpected results (716.02(b)). Note also that SEQ ID NO: 2 is referred to in the specification as an FL siRNA, not an FT siRNA. Applicant has not pointed to any evidence in the specification or elsewhere supporting unexpected results obtained with an FL siRNA.

Applicant addresses the rejection over Hyer, Uslu, Ni, and Tuschl at pages 15-17 of the response.

Applicant argues that, given the teachings of Siegmund, one of skill would not have considered providing compositions and methods involving both c-FLIP inhibitors and chemotherapeutic agents. This is unpersuasive for the reasons set forth above, i.e. Wajant suggests the combined use of c-FLIP siRNA and chemotherapeutics.

Applicant argues that one of skill would not consider substituting one of the chemotherapeutic agents recited in Ni for one recited in Uslu for combination with CH-11 treatment because Uslu taught that only certain specific chemotherapeutic agents have the desired effect with respect to sensitization to CH-11. Thus Applicant appears to argue that there would have been no reasonable expectation of achieving a synergistic effect. This is unpersuasive because no synergistic effect s required to establish a prima facie case of obviousness. All of the recited agents (CH-11, 5-FU, oxaliplatin, CPT-11, CDDP, adriamycin and etoposide) induce apoptosis. No synergistic effect is required to render obvious the combined use of CH-11 with any other chemotherapeutic agent because one of ordinary skill recognizes that there is a reasonable expectation that an increased apoptotic effect would be obtained by coadministration of different apoptosis-inducing drugs. For these reasons the rejections are maintained.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 571-

272-0762. The examiner can normally be reached Monday through Friday between the hours of 6:00 AM and 3:30. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, James (Doug) Schultz, can be reached at (571) 272-0763. The official central fax number is 571-273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

/Richard Schnizer, Ph. D./
Primary Examiner, Art Unit 1635